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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,175	07/14/2005	Peter Von Matt	TX/4-32732A	8299

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
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EXAMINER	
KOSACK, JOSEPH R	
ART UNIT	**PAPER NUMBER**
1626	

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08/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,175	VON MATT ET AL.	
	Examiner	Art Unit	
	Joseph Kosack	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 and 10-11 are pending in the instant application.

Amendments

The amendment filed June 20, 2007 has been acknowledged and has been entered into the application file.

Petition Under 37 CFR 1.144

By virtue of the petition decision of April 5, 2007, the groups are as defined in the decision, namely that Group I where R is (a) and Group II where R is (b).

Status of the Claims

Claims 1-8 and 10-11 have now been searched in their entirely as currently amended.

Previous Specification Objections

In the previous action, the abstract was objected to for not being in proper form. A new abstract has been submitted in proper form, and the objection is withdrawn.

Previous Claim Objections

Claims 1-10 were previously objected to for containing elected and non-elected subject matter. The non-elected subject matter has been cancelled and the objection is withdrawn.

Previous Claim Rejections - 35 USC § 112

Claim 10 was previously rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement and written description requirements. Applicant's amendments have alleviated the rejection, and the rejection is withdrawn.

Previous Claim Rejections - 35 USC § 103

Claims 1-10 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Albert et al. (WO 02/38561 A1).

Applicant has traversed the rejection on the grounds that it would not have been predictable that the compounds of the present application have therapeutic benefits. This is not found to be persuasive because Albert et al. teach specific examples having bicyclic structures and monocyclic structures in the R position with no apparent loss of activity ***for the same utility***. Therefore, it is only a matter of simple substitution for one of skill in the art to generate the instant compounds from the compounds of Albert et al. The rejection is maintained for claims 1-8 and 10. The rejection is withdrawn from claim 9 as that claim has been cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention is the prevention or treatment of all inflammatory and autoimmune diseases (claim 11).

The State of the Prior Art and the Predictability or Lack Thereof in the Art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:
It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Also, while the specification list several examples of diseases that are allegedly linked to with T lymphocytes and/or PKC or GSK-3β, no journal references have been provided to show the efficacy of the

mechanism of treatment. Given the broad range of diseases in the specification, a clear delineation between the inhibition of with T lymphocytes and/or PKC or GSK-3β and which diseases can be treated by the mechanism should be provided and placed in the claims. Additionally, no journal articles specific to show the correlation between T lymphocytes and/or PKC or GSK-3β and inflammatory disorders and autoimmune diseases are provided or cited within the application.

Hence, in the absence of a showing of correlation between all inflammatory and autoimmune diseases claimed as capable of treatment by mediating T lymphocytes and/or PKC or GSK-3β, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of mediating T lymphocytes and/or PKC or GSK-3β.

The Amount of Direction or Guidance Present and the Presence or Absence of Working Examples

The specification teaches that the class of compounds claimed are reactive towards T lymphocytes and/or PKC or GSK-3β. The specification also provides examples of diseases mediated by these targets, and assay procedures to identify the ability of compounds to inhibit the targets. Limited data is provided for the class of compounds, as it seems that only examples 1, 10, 39, and 41 have been tested. It cannot be readily determined if the assays or examples provide support for treatment of diseases mediated by T lymphocytes and/or PKC or GSK-3β.

The Breadth of the Claims

The breadth of the claims is the treatment of inflammatory and autoimmune diseases with the compound of claim 1 (claim 11). These diseases include specific diseases defined in page 21 of the specification, but are not limited to the listed diseases. Therefore, the claims also cover AIDS, headache, sprains, etc...

The Quantity of Experimentation Needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine not only the binding affinity of the instant compounds to the T lymphocytes and/or PKC or GSK-3β receptor, but also the ability of antagonization of T lymphocytes and/or PKC or GSK-3β to treat inflammatory and autoimmune diseases.

The Level of Skill in the Art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of claim 1 for the treatment of diseases mediated T lymphocytes and/or PKC or GSK-3β. As a result, necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome either deleting the claim or amending the claim to list specific conditions (such as inflammation, rheumatoid arthritis, etc...) and providing evidence of a correlation in the form of journal articles cited in an IDS or a declaration under 37 CFR 1.132 to show enablement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

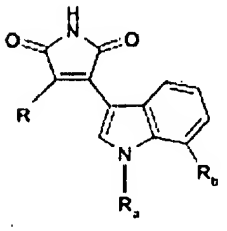
1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

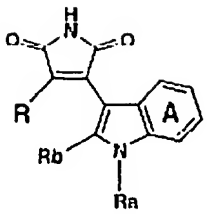
Claims 1-8 and 10-11 rejected under 35 U.S.C. 103(a) as being unpatentable over Albert et al. (WO 02/38561 A1).

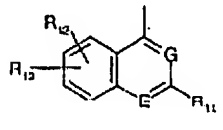
The instant invention is drawn to compounds of the formula



where: R is radical (a); R_1 is piperazine; and all other substituents are as defined. The instant invention is also drawn to its method of preparation and method of use.

Determination of the scope and content of the prior art (MPEP §2141.01)



Albert et al. teach compounds of the formula where: A is optionally substituted, Ra is H or optionally substituted C_{1-4} alkyl, Rb is H or C_{1-4} alkyl, R is  where G is CH, E is N, R_{11} is a heterocyclic residue, and R_{12} and R_{13} are optional substitutions. See pages 1-2. Albert et al. teaches specifically piperazine in the R_{11} substitution. One example is Example 163 on page 31. Albert et al. teaches the same process of forming the compounds. See page 6. Finally, Albert et al. teaches that the compounds are inhibitors of T lymphocytes and/or PKC. See pages 36-40.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Albert et al. teaches a quinoline (benzofused pyridine) and not teach a pyridine ring in the R position.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Albert et al. teaches other monocycles versus the benzofused cycles with no loss of utility and no apparent loss of activity. Specifically, Albert et al. teaches the R position to be phenyl or napthelene, and pyrimidine or quinazoline. See page 1.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to follow the synthetic scheme of Albert et al. and

pyridine for quinoline to make the claimed invention with a reasonable expectation of success. The motivation to do so is provided by Albert et al. Albert et al. teach the use of the synthesized compounds to treat various diseases mediated by T lymphocytes and/or PKC and the substitution for benzofused rings for the corresponding monocycles. See page 1 and 36-40.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

Conclusion

Claims 1-8 and 10-11 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-F 6:30 A.M. until 4:00 P.M. The examiner has every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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